DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
CENTER FOR DISEASE CONTROL
ATLANTA, GEORGIA

MINUTES OF MEETING

Immunization Practices Advisory Committee
October 25-26, 1979

The Immunization Practices Advisory Committee (ACIP) met in Conference Room 207, Center for Disease Control, Atlanta, Georgia, on October 25-26, 1979 Those in attendance are listed below:

COMMITTEE MEMBERS PRESENT

Dr. Thomas M. Vernon, Jr., Chairman
Dr. James Chin
Dr. Suzanne E. Dandoy
Dr. John B. De Hoff
Dr. Maxine Hayes
Dr. Edwin D. Kilbourne
Dr. William M. Marine
Dr. Jay P. Sanford
Dr. Gary R. Smith
Dr. Catherine M. Wilfert

Liaison Representatives

Dr. Edward A. Mortimer, Jr. (AAP)
Dr. Asher J. Finkel (AMA)
Dr. J.M.S. Dixon (NACI)

COMMITTEE MEMBERS ABSENT

Ex-Officio Members

Dr. William S. Jordan, Jr. (NIH)
Represented by Dr. James C. Hill
Dr. Harry Meyer, Jr. (Bur/Biologics)
Represented by Dr. Paul Parkman

STAFF PRESENT

Office of Center Director

Dr. William H. Foege, Director
Dr. J. Donald Millar, Executive Secretary, ACIP

Office of General Counsel

Mr. Charles Gozonsky

Bureau of State Services

Dr. Roger Bernier
Dr. A. D. Brandling-Bennett
Dr. Frank De Stefano
Dr. Alan Hinman
Dr. John Kobayashi
Dr. Timothy Nolan
Dr. Marjorie Pollack

Bureau of Epidemiology

Dr. Larry Anderson
Dr. Claire Broome
Dr. Donald Francis
Dr. David Fraser
Dr. Marie Griffin (New Jersey SHD)
Dr. Peter Katona
Dr. Melinda Moore
Dr. Jeffrey J. Sacks (S.C. SHD)
Dr. Lawrence Schonberger
Dr. Mary Serdula (Hawaii SHD)
Dr. Kathryn Shands
Dr. Steve Thacker
Dr. William Winkler

Bureau of Laboratories

Dr. Dick Facklam
Dr. Alan Kendal
Dr. Gary Noble

Bureau of Smallpox Eradication

Dr. Jason Weisfeld

OTHERS PRESENT

Dr. Robert Austrian, Univ. of Pa.
Dr. J. Banduniak, Merck Sharp & Dohme (MSD)
Dr. David W. Bentley, Monroe Community Hospital, Rochester, N.Y.
Dr. W. F. Daly, Lederle Laboratories
Dr. Alan Gray, MSD
Dr. Maurice R. Hilleman, MSD
Dr. William McIntosh, MSD
Ms. Arlene McLean, MSD
Dr. Aubrey S. Outschoorn, US Pharmacopeia
Ms. Linda Paulin, MSD
Dr. D. B. Reynolds, Connaught Laboratories
Dr. Michael Riddiough, Office of Technology Assessment, U.S. Congress (OTA)
Dr. Gerald Schiffman, State Univ. of N.Y.
Dr. Charles Vaughn, Wyeth Laboratories
Dr. Jane Willems, VA Scholar, former OTA

Chairman Vernon opened the meeting at 8:30 a.m., October 25, and introduced the new members of the ACIP: Drs. Smith, Chin, De Hoff, and Marine. He introduced Dr. Millar, the new Executive Secretary of the Committee, who announced that a ceremony would be held at CDC on the afternoon of October 26 to commemorate the certification of the horn of Africa as free of smallpox. He noted that the last naturally occurring case of smallpox occurred in Somalia October 26, 1977, and that teams of international experts had recently certified Kenya, Ethiopia, Djibouti, and Somalia (the last infected country) as free of the disease.

Dr. Hinman announced that based on provisional data, President Carter's national immunization initiative, which had begun in October 1977, had reached its objectives of immunizing 90% or more of school children against polio, diphtheria, pertussis, tetanus, and measles. In addition, these data indicated that 84% were immunized against rubella.

Poliomyelitis

Chairman Vernon opened discussion on the draft revised statement on the prevention of poliomyelitis. He asked Dr. Moore to summarize the recent epidemiological situation. She described one fully immunized child from Ohio who in 1978 developed bulbar poliomyelitis and died. This was the first documented instance in the United States of paralytic disease in a person who had received 3 or more doses of trivalent Oral Polio Vaccine. She also described results of epidemiologic studies in Lancaster, Pennsylvania, during the recent polio epidemic among the Amish. In 75 school children in affected areas, there was no evidence of wild poliovirus excretion. Two children were excreting polioviruses presumed to be vaccine strains; one of these had been in contact with a recent vaccinee. In a serosurvey of 103 persons claiming never to have been vaccinated, only 2 were actually seronegative to all 3 poliovirus types, whereas 65% had measurable antibody titers to all types. Of persons attending one of the county-wide vaccination clinics, 46% felt that they had already been fully immunized against poliomyelitis (and most gave historical information to support this). Nevertheless, they sought an additional dose at the clinic.

Discussion next turned to the draft polio statement. Dr. Chin proposed rewording the section dealing with the need for additional doses of vaccine every 5 years among persons thought to be at high risk, and for the management of single-case "outbreaks." There was discussion of the evidence for any need of repeated doses of IPV every 5 years in children. Dr. Hinman was asked to make the appropriate changes in the text; subsequently, an amended draft was approved by the Committee for publication in the Morbidity and Mortality Weekly Report the next week.

Rubella

Following a break, Dr. Parkman discussed a study (by Balfour; American Journal of Diseases of Children 132:573, June 1978) reporting that 32% of rubella-vaccinated children studied had no detectable antibody to rubella. These observations seem to question the efficacy of rubella vaccination. Subsequently Dr. Ennis, of the Bureau of Biologics (BoB) in collaboration with Dr. Balfour, tested the same sera by techniques usually used at BoB. Results indicate that the tests used by BoB were 2- to 4-fold more sensitive than those by Balfour. Dr. Parkman concluded that there was no compelling evidence for doubting the efficacy of rubella immunization.

Dr. Brandling-Bennett reviewed 4 cases (since 1977) of apparent congenital rubella syndrome among offspring of mothers inadvertently receiving rubella vaccine during pregnancy. In each there was laboratory and/or epidemiologic evidence suggesting that the mother was infected with wild rubella virus as well as vaccine virus. There are still no known cases in which vaccine virus is unequivocally implicated as the cause of the congenital rubella syndrome.

The Committee did not feel it necessary to make changes in the current recommendation on Rubella Vaccine.

Rabies

Dr. Vernon called on Dr. Winkler to introduce a draft statement on rabies vaccines. Because of the significant risks of undesirable side effects of currently used antirabies agents, CDC and the State health departments have attempted to reduce the number of unnecessary post-exposure treatments in recent years. However, a new and safer human diploid cell rabies vaccine (HDCV) is expected to be licensed before January 1, 1980; its availability may increase the number of unnecessary treatments. Initially the vaccine supply will be limited (about 50,000 doses), and it is expected that State health departments will receive high priority for its distribution.

There was considerable discussion of the draft. Dr. Dandoy suggested that information about the agents be presented in 2 general categories: "Active Immunizing Agents" and "Passive Immunizing Agents," and that the paragraphs on the management of biting animals be separated from those on immunization. Dr. Sanford and others suggested that the summary table be amended to include the new vaccine and perhaps more detail in order to reduce potential ambiguities. Enumerating those areas in the world where there is a "high risk" of exposure was felt desirable.

Dr. Parkman noted that the proposed recommendation differed from the current recommendation of the World Health Organization for HDCV vaccines similar to the one to be available in the United States. The WHO advises a 6-dose schedule (days 0, 3, 7, 14, 28, and 90 after exposure) in contrast to the 5-dose schedule (days 0, 3, 7, 14, and 28) recommended in the draft. Dr. Winkler replied that immunologic data, which indicated that even a 4-dose schedule (days 0, 7, 14, and 28 after exposure) was probably adequate, justified the recommendation for a 5-dose regimen.

There was considerable discussion of the need for preexposure vaccination for American visitors to "high-risk" countries, especially children. Dr. Sanford pointed out that the HDCV offered a safe and effective preimmunizing agent, whereas postexposure protection available in most such countries would be the Pasteur neurotropic vaccine, which is hazardous. It seemed prudent, therefore, to be liberal in recommending preexposure vaccination of children expected to be exposed in such circumstances.

The Chairman requested that a second draft document be prepared by Dr. Winkler and his staff incorporating the suggested changes, forwarded for editorial review to Dr. Millar, and distributed for discussion by a subcommittee including Drs. Vernon, Chin, and Sanford.

Pneumococcal Vaccines

After lunch the Chairman introduced Dr. Fraser, who moderated a special session on pneumococcal vaccines consisting of 5 formal presentations and considerable discussion. Dr. Austrian, who has worked on development of pneumococcal vaccines in the United States, was present and contributed substantially to the discussion.

Dr. Hilleman summarized data on the antibody response to pneumococcal vaccines indicating that the dose presently recommended (50 mcg of each of the 14 pneumococcal components per dose of vaccine) seemed appropriate. Vaccine efficacy has been 76-100% in various studies. The immune response of children from infancy to 14 years of age was not as good as that of adults, which is excellent. Marked local and general reactions occur in a high proportion of subjects receiving a repeat dose of vaccine within 1 to 1-1/2 years. He presented data showing that pneumococcal vaccine and whole-virus influenza vaccine had been administered simultaneously in separate sites without a loss of efficacy nor increased side effects. No studies on the use of split-virus flu vaccines in this way have been reported. He made a strong plea for much more widespread use of the pneumococcal vaccine in "high-risk" groups, of whom "only 1/20" now receive the vaccines.

Dr. Bentley presented data on studies of pneumonia and pneumococcal vaccines in the Monroe Community Hospital system. He noted that patients entering these institutions had a high risk of acquiring pneumonia especially during the first 400 days after admission. However, only 13-22% of the pneumonias were due to pneumococci, and only 75% of these were due to strains included in the pneumococcal vaccine. Most pneumonias were due to mixed flora. Indeed, he had been somewhat anxious that the use of pneumococcal vaccines to prevent some forms of pneumonia would result in a higher incidence of other types, such as those due to Gram-negative agents. The vaccine proved quite effective in preventing the disease due to the pneumococcal types in the vaccine, but the overall impact of immunization on the rate of pneumonias was not clear.

Drs. Riddiough and Willems of the Office of Technology Assessment discussed a cost effectiveness analysis of the use of pneumococcal vaccines. Unfortunately, the actual value of several crucial variables is not known. However, it appears that the ratios were more favorable for older persons. In discussing this presentation, Dr. Chin noted that the State Legislature of California has initiated a limited program to provide vaccine to persons meeting the risk criteria defined in the existing ACIP statement on pneumococcal vaccines.

Dr. Broome then presented results of a national surveillance system monitoring the serotypes of 573 pneumococcal isolates recovered from patients in 46 hospitals. Results show that about 70% of the total isolates were of the serotypes included in the vaccine, whereas 15% are "related" serotypes. She also looked at serotype distribution in pneumococcal infections among persons who have received the pneumococcal vaccine. There have been only 20 such isolates received so far. These isolates suggest an efficacy of only 25-30% for the vaccine in this group consisting primarily of individuals with significant underlying disease among whom efficacy would not be expected to be high. Dr. Fraser noted that important data will be available in the coming months.

After reviewing the current statement, the Committee felt no need to change the recommendations on pneumococcal vaccines. However, Dr. Sanford suggested that new data on the simultaneous administration of pneumococcal vaccines and influenza vaccines be reflected in the next revision of the statement on influenza immunization.

Mumps

The existing statement on mumps vaccine was reviewed for possible changes. Several suggestions were made. Dr. Hinman was requested to prepare recommended changes to cover these points for review by the Committee by mail.

Measles

Dr. Bernier and Dr. Hinman summarized the current epidemiologic status of measles in the United States. Measles is at an all-time low as measured by several indices. Intensive surveillance is being conducted in HEW Regions VII and VIII; in the 10 States only 33 cases have been found this summer. Military posts and day-care centers appear to be principal sources of continuing transmission in communities. Although refugees have brought measles into the United States, they have not proven a major source of spread beyond the refugee population. Of the Nation's 52 reporting areas (States and major metropolitan areas) 81% have had at least one 4-week period free of measles during the current year.

Dr. Vernon noted that strict enforcement of laws mandating the vaccination of 15-month-old children in day-care centers would perhaps protect the younger children as well.

Dr. Dixon reported that in Canada a national policy statement has been drawn up reinforcing the idea of beginning vaccination at 12 months of age and recommending school entry laws in all provinces, if necessary.

The Committee did not feel it necessary to revise the existing measles recommendation at this time.

Influenza

Dr. Kendal summarized influenza virus activity in the southern hemisphere during the past summer, noting isolates in Australia of H1N1, and in Southeast Asia of both H1N1 and H3N2 strains. However, most influenza seemed to have been influenza B, reported exclusively among children. Because the surveillance systems were oriented primarily to children, this was of dubious significance. Dr. Chin asked whether or not we had influenza B in the United States, and whether there was any evidence of antigenic "drift." Dr. Kendal responded that influenza B was active in Hawaii from July on, and there was a preliminary report of an influenza B isolate in Texas. A proportion of the isolates are similar to B/Hong Kong/5/72, while others seemed poorly reactive to this, possibly due to avidity. Whether or not this is evidence of a drift is questionable. To date there is no clear indication for adding a "more contemporary" strain to the recommended vaccines, although this is being considered.

Dr. Noble reviewed the results of influenza vaccine trials at the University of Georgia indicating a 50% vaccine efficacy for A/USSR/77(H1N1) vaccine against infections with A/Brazil/78(H1N1) virus. Dr. Hinman noted that there is still an influenza vaccination program, and that this winter both last year's vaccine as well as the new formulation will be used. Dr. Noble summarized the influenza surveillance system planned for this year, noting changes from the previous system. Dr. Thacker discussed an alternative method of analyzing influenza mortality data which might improve on some of the problems noted with the present regression model. The alternative method, known as an "autoregressive integrative moving average," would permit earlier updating of the expected number of deaths in the absence of influenza.

Recommendations on influenza immunization will be dealt with in January.

Hepatitis

The Committee heard a comprehensive review of developments in the field by Dr. Francis. He noted that hepatitis A appears to behave as an enterovirus; that day-care centers, especially those with "kids in diapers," represent foci of intense transmission; that employees of such centers are at increased risk; and that the availability of a live attenuated vaccine now being developed in the United States, is probably "still years away."

The hepatitis B virus, which probably accounts for 30-40% of the hepatitis in the United States, cannot now be grown. Nonetheless, we have considerable understanding of its epidemiology. A killed virus vaccine developed by Merck, Sharp & Dohme is estimated to provide 95-97% seroconversions with few side effects. This vaccine will shortly be evaluated by CDC in large-scale trials among a group of male subjects whose annual infection rate with hepatitis B is about 25%. The Pasteur Institute has initiated control trials of its vaccine in employees of dialysis units and expects to market the vaccine soon.

Regarding "non-A, non-B" hepatitis, reliable laboratory tests are not yet available. Studies in chimpanzees suggest that "non-A, non-B" will turn out to be at least two separate agents, C and D.

Regarding postexposure passive protection, Dr. Francis expressed the growing conviction that HBIG is not a highly effective preventive modality for hepatitis B virus infection. It is more expensive, offers only marginal benefits, and is more difficult to get in a timely fashion than ISG. There have been reported benefits of using HBIG to protect infants born of hepatitis B-carrier mothers; additional studies are being done to confirm this. The benefit of using HBIG immunization in protecting the spouses of individuals with acute infections of hepatitis B is also being questioned. These conflicting findings may be due to the pathogenesis of hepatitis B, which seems to be an immunologically induced disease, rather than one caused by a cytopathic effect of the virus.

After hearing the presentation by Dr. Francis, the Committee decided that it would like to begin a review and updating of the statement, "Immune Globulins for Protection Against Viral Hepatitis." The Chairman requested that proposed amendments be drafted by staff of the Hepatitis Laboratory in Phoenix for consideration by the Committee in due course.

DTP

Drs. Pollack and Hinman summarized results of the recently implemented surveillance system for adverse reactions following immunizations. Since May 1978, 31 deaths have occurred in infants who had received DTP vaccine. Fifteen occurred within 24 hours of immunization; 3 occurred more than 22 days after immunization. There appears to be no association with specific vaccine products or lots.

Dr. Chin requested that CDC pursue the results of any studies going on in England at present in view of the diminished use of DTP in infancy there.

Dr. Parkman read the package insert proposed by Wyeth Laboratories for inclusion in its DTP vaccine.

Chairman's Summary for CDC Director

After lunch on October 26, Dr. Foege joined the meeting, and Dr. Vernon summarized for him the results of the Committee's deliberations over the previous day-and-a-half. (It is expected that summaries for the CDC Director will become a regular part of ACIP agendas.) Dr. Vernon summarized all agenda items except the special session on pneumococcal vaccines, which was summarized by Dr. Sanford.

In discussing polio vaccines, Dr. Foege asked, "Under what circumstances would you recommend IPV as the basic immunizing agent in the United States?" Several Committee members commented on the question, in general asserting that when the delivery of vaccine to children in the United States approximates the nearly universal delivery in Scandinavia, such a recommendation should be considered.

In commenting on the session on pneumococcal vaccines, Dr. Foege asked how vigorously CDC should encourage the use of these vaccines. Several Committee members responded generally that the current recommendations permitted immunization of "high-risk" individuals for whom the vaccine seemed to offer benefits. In contrast to its feeling about influenza immunization, however, the Committee had little enthusiasm for aggressive programs to vaccinate the healthy elderly with pneumococcal vaccines.

Regarding measles immunization, Dr. Foege asked if the Committee could say something to encourage all State health departments to aggressively pursue measles elimination. Committee members felt that the Committee should encourage States to pursue special searches and other special activities to the extent possible and that the complete elimination of indigenous measles was certainly a worthy objective.

In discussions about the hepatitis session, Dr. Hayes noted that CDC needs to consider ways by which the licensing requirements for day-care centers might be "tightened up" in view of their emerging role as foci for the transmission of several diseases.

In closing, Dr. Foege complimented the Committee, noting the major impact of its deliberations and activities on CDC. He expected that impact to continue and predicted that within 5 years, because of vaccines now being developed, that the Committee would produce recommendations on immunization against such agents as rotavirus, hepatitis, leprosy, and malaria.

It was agreed that the next meeting of the ACIP would be held in Bethesda, Maryland, at the Uniformed Services Medical School on January 21, 1980.

the meeting was adjourned at 2:30 p.m., October 26.

I hereby certify that, to the best of my knowledge, the foregoing summary of minutes is accurate and complete.

Thomas K. Vernon M.D. 11-28-79

Chairman Date

Executive Secretary Date